REMARKS

Applicants acknowledge receipt of an Office Action dated June 18, 2007. Reconsideration of the present application is respectfully requested in view of the foregoing amendments and the remarks which follow.

I. Status of the claims

No claims are amended. Claims 1-8, 10, 15 and 18 were previously canceled. Claims 19-25 are new, and present substantially identical claims as 9, 11-14, 16 and 17, except that the term "PM-1" has been deleted from the preamble. These new claims do not introduce new matter. Following entry of new claims 19-25, claims 9, 11-14, 16-17, and 19-25 are pending in the application, with claims 9, 13, 19 and 22 being independent.

II. Interview with the Examiner.

Applicants thank the Examiner for extending the courtesy of an interview, which occurred between the Examiner and Applicants' representatives on November 28, 2007. The following amendments and remarks follow from the interview.

III. Objection to the Specification

At pages 2-3 (§ 3) of the Office Action, the Examiner has reasserted the prior objection to the specification for Applicants' incorporation by reference from WO 92/19759. Applicants respectfully assert that such incorporation by reference is proper, and wish to address the different aspects of the continuing objection. These aspects might be usefully reduced to: (a) confusion as to why certain patent documents are cited and for what purpose; (b) where can the material be found in the document sought to be incorporated by reference; and (c) whether Applicants are entitled to incorporate this information by reference.

(a) Appendix A provides an overview of the applications and patents relevant to the present issue

In case there is some confusion, Applicants have provided Appendix A, which sets forth the relationship of the various cases at issue. The pending application, U.S. Application No. 09/156,125, is a continuation of the application which matured into U.S. Patent No. 5,888,510, which is the U.S. National Phase of PCT/JP1995/00144 (published as WO 96/11020). PCT/JP1995/00144 incorporates by reference WO 92/19759. WO 92/19759 is the publication of PCT/JP1992/00544, which entered U.S. National Phase and, ultimately, matured into U.S. Patent No. 5,759,965. Applicants also wish to bring to the Examiner's attention the claims at issue in the different English-language applications. These claims have been partially reproduced in Appendix A.

(i) U.S. Patent No. 5,759,965 is directed to a genus of reshaped human antibodies to the human IL-6 receptor, and defines specific structural features of the genus.

(ii) U.S. Patent No. 5,888,510 is directed to a method for inhibiting synovial growth by administering an interleukin-6 antagonist

(iii) The present application claims a method for inhibiting synovial cell growth by administering a humanized antibody against the IL-6 receptor, and defines specific structural features of the genus. This genus is taken directly from that which is described and claimed in U.S. Patent No. 5,759,965. Thus, in the present application the method of U.S. Patent No. 5,888,510 is practiced with the antibodies of U.S. Patent No. 5,759,965.

Applicants have made previous reference to U.S. Patent No. 5,759,965 because it is the English translation of WO 92/19759, which is incorporated by reference into the present application, and because the claims in U.S. Patent No. 5,759,965, are directly relevant to those pending in the present application.

(b) Location within WO 92/19759 of the information sought to be incorporated by reference

The Examiner has previous objected to Applicants' reference to U.S. Patent No. 5,759,965, and so Applicants will refer instead to the PCT publication WO 92/19759 and to the translation provided and of record in this case.

In WO 92/19759, the L chain C region is defined as Cκ and the H chain C region is defined as Cγ. The use of the constant region Cκ for the construction of the L chain of humanized PM-1 antibody (hPM-1) is described on page 74, lines 10 to 13 of WO 92/19759 (page 58, lines 19 to 22 of the translation), and the use of the constant region "Cγ" for the construction of H chain of hPM-1 is described on page 74, lines 13 to 16 of WO 92/19759 (page 58, lines 22 to 25 of the translation). Please note that the constant region "Cκ" of L chain human antibody and the constant region "Cγ" of H chain of human antibody are well known in the art. Regarding CDR and FR of the H chain, the amino acid sequences of the CDRs and FRs of H chain V region are described in Table 3, on pages 24 to 25 of WO 92/19759 (pages 20 to 21 of the translation). The amino acid sequences of CDRs and FRs of L chain V region are described in Table 2 on page 22 of WO 92/19759 (pages 17 to 18 of the translation).

(c) Applicants are entitled to incorporate this material by reference.

The Examiner's objections do not appear to be based on whether incorporation by reference is allowed as a general matter (which it is *see, e.g.* MPEP § 2163.07), but what Applicants are entitled to incorporate by reference. At two locations in the specification, Applicants incorporate by reference the relevant subject matter. At page 6, lines 19-29 of the present application (page 7, lines 1-11, in WO 96/11020) the PM-1 antibody/antibodies of Hirata *et al.*, J. Immunol. 143:2900-2906, 1989 is/are incorporated by reference. Hirata *et al.* was made of record in the Information Disclosure Statement filed January 9, 2001. Next, at page 10, line 29 to page 11, line 2 of the present application (page 11, lines 12-18 in WO 96/11020) the humanized PM-1 antibody/antibodies of WO 92/19759 is/are incorporated by reference.

One aspect of the Examiner's objection is that the specification refers to PM-1 and hPM-1 in the singular form. Applicants provide herewith Appendix B, an executed declaration by a native Japanese speaker, demonstrating that the original Japanese text can be understood to refer to PM-1 and hPM-1 as plural forms. The Examiner has noted that the specification is, itself, a certified translation. Applicants do not disagree that the specification as filed is a certified translation, and agree that it is a correct translation. However, accepting that the singular form is a correct translation does not, *per se*, mean that a translation to the

plural form is incorrect. It is well known that words and concepts imperfectly correspond between languages, such that multiple correct translations are possible for any one phrase, and any one translation may not perfectly reflect the original text. Appendix B does not mean that the original English translation is incorrect, but that it would be incorrect to read a specific meaning into the text when such meaning is lacking in the original. Therefore, the Examiner's reliance on a specific meaning is actually contradicted by the evidence.

Moreover, even if PM-1 is a specific murine monoclonal antibody, it is well known that many possible antibodies can result from the process of "humanizing" a murine antibody, reflecting the myriad choices available to make a chimeric construct. This is exemplified in WO 92/19759, which describes the various fragments used in making humanized PM-1, and describes various different humanized variants. For example, Table 2 in the English translation of WO 92/19759 is titled "Design of two different versions of reshaped human PM-1 L chain V region," while Table 3 is "Design of six different versions of reshaped human PM-1 H chain V region." These alternatives have been sought to be incorporated by reference into the present application.

At page 3, first paragraph, of the Office Action, the Examiner refers to Reference Examples 1 and 2, as support for a single PM-1 murine hybridoma. Applicants note, however, that the preceding pages, from page 8 onwards, are replete with detailed information on the construction of humanized PM-1 antibodies from, and comparison of the various humanized variants to determine which have superior properties. Thus, the existence of a single, original murine hybridoma does not similarly limit the possible humanized variants to one.

(d) Summary

Applicants respectfully assert that they have overcome the Examiner's objection, and request reconsideration and entry of the amendment to the specification. Applicants also request that the Examiner contact the undersigned if it is believed that editorial amendments are necessary to enter the text into the specification.

IV. Rejections Under 35 U.S.C. § 112

(a) Response to the Office Action

At pages 4-5 (§§ 4-5) of the Office Action, the Examiner has maintained the rejection of claims 9, 11-14, and 16-17 under 35 U.S.C. § 112, first paragraph, written description. Applicants respectfully traverse, for reasons of record.

The central issue, in the opinion of the Examiner, is whether Applicants intended to incorporate by reference a genus of hPM-1 antibodies, or a single hPM-1 antibody. Applicants believe that this issue has been addressed in Section III, above.

Nonetheless, Applicants maintain the written description requirement is met by art that was known to the person of ordinary skill at the time of filing. WO 92/19759 and Hirata *et al.* were available at the time of filing the present application, and were specifically referenced in the specification.

The Examiner challenges that Applicants were in possession of the genus of antibodies sought to be claimed. Since WO 92/19759 and Hirata *et al.* were published prior to the filing date of the present application, Applicants were in possession of that which is described in these references. Additionally, since both WO 92/19759 and WO 96/11020 are listed on their face as assigned to Chugai Seiyaku Kabushiki Kaisha, Applicants were in actual possession of the genus of antibodies described in WO 92/19759 *prior* to the filing date of the present invention.

The Examiner also challenges the relevance of *Falkner v Inglis* and *Capon v. Eshhar,* because (it is asserted) these cases involve DNA sequences, and because the court in *Capon* was mostly concerned with enablement. The fact that the *Capon* court was mostly concerned with enablement is irrelevant. *Capon* is highly relevant to written description, and is cited in the MPEP § 2163 for this purpose. Not only is *Capon* legally relevant, it is also factually analogous. *Capon* involved chimeric antibodies, and sought to incorporate by reference DNA sequences that were already known in the art. The present application involves chimeric antibodies, and seeks to incorporate by reference amino acid sequences that were already known in the art. The distinction between DNA in *Capon* and the amino acids here is a distinction without merit.

(b) New claims 19-25

Applicants wish to promptly proceed towards allowance. To expedite allowance, new claims 19-25 are presented, with almost identical subject matter as claims 9, 11-14, and 16-17. Claims 19-25, however, do not recite hPM-1. Therefore, these claims overcome rejections based on the Examiner's assertion that it difficult to determine whether a single hPM-1 antibodies, or multiple hPM-1 antibodies, are properly incorporated by reference.

(c) Summary

For at least these reasons, Applicants respectfully believe that the rejections are overcome and request reconsideration and allowance of the pending claims.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that all of the pending claims are now in condition for allowance. An early notice to this effect is earnestly solicited. If there are any questions regarding the application, the Examiner is invited to contact the undersigned at the number below.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are

needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Dec. 17, 2007

By _____

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